Available online at www.sciencedirect.com
ScienceDirect
Physica A 387 (2008) 1200–1204
PHYSICA A
www.elsevier.com/locate/physa

A note on the effects of replenishment of depleted cells on HIV infection dynamics: A graph-theoretic approach

Simon Mukwembi*

School of Mathematical Sciences, University of KwaZulu-Natal, Westville Campus, P Bag X54001, Durban, South Africa

Received 11 February 2007; received in revised form 8 May 2007
Available online 22 October 2007

Abstract

We study the effects of the rate of replacement of dead cells by either healthy cells or by infected cells on HIV infection dynamics through a graph-theoretic approach. Our framework takes into account a reasonable amount of the immune action to any pathogen and the local cell interactions that occur in the lymph nodes. Our results, in an extremal case where dead cells are highly likely to be replaced by healthy cells, show that all cells become healthy in a finite number of steps of given order and infection stops propagating. Further, for this extremal case, we give an algebraic formula for the number of infected cells at any given time in the HIV progression. We also find a sufficient condition, determined by dead cell replacement rate, which guarantees that an infected patient is continually positive, and give bounds on the number of infected, healthy and dead cells at any given time. We apply our theoretical results to a recently proposed model of the HIV infection dynamics.

PACS: 02.10.Eb; 02.10.-v; 87.10.+e; 89.70+c

Keywords: Graph; Lymph node; HIV

1. Introduction

Experimental evidence [3,8] supports that vast majority of HIV infection occurs in the lymph nodes, where HIV-infectible $CD4^+$ T cells are densely packed. Only about 2% of the T cells are located in the blood. A lymph node has a mesh structure with different sites or voids which are potential sites of cells. It has been suggested [9,6] that viral propagation is determined purely by the lymph node geometry. Numerous researchers have interpreted the mesh structure of the lymph node differently; Refs. [10,7,1] depict the mesh structure as a square lattice, whereas Refs. [9, 6] approximate the mesh structure by a simple three-dimensional cubic lattice. The sites of the lymph node have three states; a site can be occupied by a healthy cell, infected cell or a dead cell. It is folklore that viral populations can only grow by infecting and using a host cell's machinery and metabolism to replicate. In the HIV replicative cycle, the virus enters the cell via the latter's receptors. This is followed by the release of the HIV capsid into the cell which in turn activates reverse transcription culminating in at least one mutation of the virus and hence producing a new

* Tel.: +27 312608167, +27 733453585; fax: +27 312607806.
E-mail address: mukwembi@ukzn.ac.za.

0378-4371/$ - see front matter
doi:10.1016/j.physa.2007.10.038

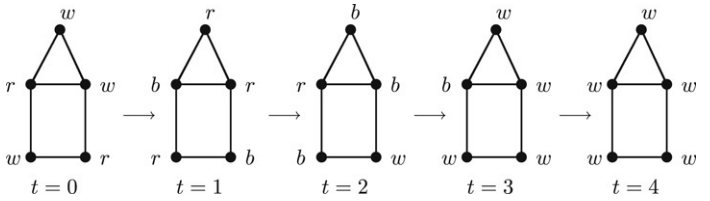

Fig. 1. Example for applying the rules with $R = 3$; w = white, r = red, b = black.

strain of the virus. The cell then dies releasing the new strain of virions all of which attach to and infect neighbouring cells [9].

The propagation of the virus in the discrete time steps is governed by the following transitional rules.

*R*1: *A healthy cell becomes infected if it has at least one infected neighbour; otherwise it stays healthy.* This rule mimics the spread of HIV infection by contact [10,9,6] and, in conjunction with *R2* below, incorporates the virus construction and its replication.

*R*2: *An infected cell dies in the next time step.* This rule simulates the depletion of infected cells by the immune action [10,9,6] or direct killing of the cell by the virus.

*R*3: *A dead cell is replaced by an infected cell if it has at least R infected neighbours; otherwise it is replaced by a healthy cell.* This rule is justified by the fact that sites with dead cells are repopulated by diffusion or division of neighbouring cells or by activation of latent infected cells [10,9]. Therefore, the status of neighbouring cells of a dead cell influences the status of the replacing cell.

The initial configuration is composed of healthy cells with a small fraction of infected cells. In this paper we investigate, using graph-theoretic methods, how the changes in R determine the propagation dynamics of the HIV virus.

2. Results

A *graph* $G = (V, E)$ consists of a finite set $V = V(G)$ of *vertices* together with a set $E = E(G)$ of *edges* joining certain pairs of vertices of G. The *degree* $\deg(v)$ of a vertex v of G is the number of edges incident with v and the *minimum degree* $\delta(G)$ of G is the minimum of the degree of the vertices in G. The *distance* $d(u, v)$ between vertices u and v in G is defined as the length of a shortest path joining u and v in G. For a subset $S \subseteq V(G)$ and a vertex v of G the distance $d(v, S)$ between v and S is defined as the minimum value of $d(v, x)$, $x \in S$. The *wheel graph* is a graph obtained by joining a new vertex to every vertex of the cycle graph.

We model the above situation by a graph G as follows. The vertex set of G is the set of sites of the lymph nodes and two vertices are joined by an edge if and only if the corresponding sites in the lymph nodes are neighbours. We arbitrarily color the vertices of G using three colors, white, red and black. The colors signify a site of the lymph node occupied by a healthy, infected and dead cell, respectively. Now consider the following game played on G. A move consists of an update of the colors of the vertices in a synchronized parallel way, according to the following rules:

*G*1: A *white* vertex changes its color to red if it has at least one red neighbour.

*G*2: A *red* vertex changes its color to black.

*G*3: A *black* vertex is colored red if it has at least R red neighbours; otherwise it is colored white.

Clearly, $0 \leq R \leq |V| - 1$. Initially at time 0 some vertices of G are colored white and some red, and no black vertices are present. For an example, see Fig. 1.

Here and in the sequel S is a subset of V consisting of all vertices of G colored red in the initial configuration and s is the cardinality of S. Note that in practice, S represents the set of infected sites in the initial contamination. Further, for each discrete time t, $r(t)$, $w(t)$, $b(t)$ are the numbers of vertices colored red, white and black respectively, at time t. So for example, if $S = V$, then $r(t) = 0$ for all $t \geq 1$. We also use the following notations. The integer $e = e(S)$ is the maximum value of $d(x, S)$, $x \in V$. For each integer $i = 0, 1, 2, \ldots, e$, let N_i denote the set $N_i = \{x \in V \mid d(x, S) = i\}$ and k_i be its cardinality. So for $t > e$, $N_t = \emptyset$. It is elementary to show that for $i \neq j$, $N_i \cap N_j = \emptyset$ and that no vertex in N_i has a neighbour in N_{i+2}, $i = 0, 1, \ldots, e - 2$. We remark here that if more properties of G, such as degree conditions, are known, then more can be said about the k_is. For a vertex v, $c_t(v)$ denotes the color of v at time t. If $B \subseteq V$ is such that all its vertices have the same color y, say, at time t, we write $c_t(B) = y$.